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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,666	03/12/2007	Kenneth Powell	NV2-018US	2807

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EXAMINER	
PIHONAK, SARAH	

ART UNIT	PAPER NUMBER
1627	

MAIL DATE	DELIVERY MODE
12/20/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,666	POWELL ET AL.	
	Examiner	Art Unit	
	SARAH PIHONAK	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-22 and 24-38* is/are pending in the application.

5a) Of the above claim(s) *3,6,7,25,32,33 and 36-38* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1,2,4,5,8-22,24,26-31,34 and 35* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application, filed on 3/12/2007, is a national stage entry of PCT/GB05/01018, filed on 3/18/2005.

Priority

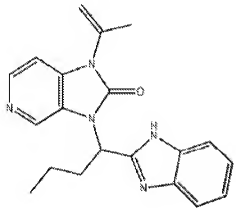
A claim for foreign priority to Application No. 0406282.4, filed on 3/19/2004, has previously been acknowledged.

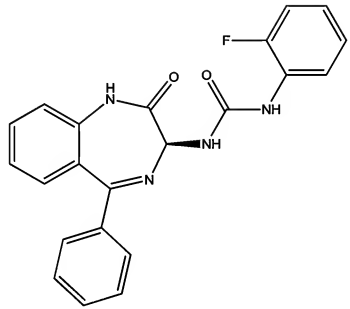
Request for Continued Examination

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/13/2010 has been entered.

Response to Remarks

2. The examiner thanks the Applicants for providing further clarification of the previously elected species. The Applicants have reiterated the elected species for (a) and (b) which are shown below, respectively:





(S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea .

The rejection under 35 USC 103(a) as being unpatentable over Yu et. al., in view of Carter et. al. is withdrawn in consideration of Applicants' arguments and clarification of the elected species of formula (I). The elected species of (a) has been found to be free of the prior art. Therefore, the search was expanded to other species of formula (I). A modified rejection under 35 USC 103(a) over Yu et. al. in view of Carter et. al. has been made, in consideration of the amended claims, which will be discussed in the office action.

The Applicants have further traversed the restriction requirement made in the office action 5/6/2009, and have submitted that unity of invention is not lacking, as the claimed composition is novel over the prior art. The examiner respectfully disagrees, as the claimed composition comprised of a compound of formula (I) and the elected benzodiazepine compound, (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea, would have been prima facie obvious to one of ordinary skill in the art in consideration of the teachings of Church et. al., WO 98/45275, in view of Carter et. al., WO 2004/026843. Church et. al. teaches compounds of formula (I) as inhibitors of RSV, while Carter et. al. teaches the elected compound, (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea, also as an inhibitor of RSV. Therefore, it would have been prima facie obvious for one of ordinary skill in the art to have combined these compounds in a pharmaceutical composition, as they are both taught to have utility for treating RSV. The restriction requirement and species election requirement were proper and are maintained. A new rejection under 35 USC 103(a) over the claims has been made in consideration of the teachings of Church et. al. and Carter et. al., which will be discussed in detail in the office action.

The rejection for obviousness type double patenting over the claims of 10/593382 is withdrawn as application 10/593382 has been abandoned. New rejections for obviousness type double patenting have been made, which will be discussed in detail in the office action.

Claims 1-22, 24-38 are pending as of the reply filed on 9/29/2011. Claims 25, 32, 33, and 36-38 were previously withdrawn from consideration, due to the restriction requirement and election. The examiner also notes that claims 3, 6 and 7 do not read on the elected species for component (b), as these claims are directed to the composition according to claim 2, wherein the compound of formula (V) of claim 2 is defined by R^3=halogen, hydroxyl, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkylthio, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, amino, mono(C_{1-4} alkyl)amino, or di(C_{1-4})alkyl)amino, etc. The elected species for component (b), (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea of formula (V) of claim 2 has n=0; therefore, R^3 is not present. Claims 3, 6-7, 25, 32, 33, and 36-38 are as such withdrawn from consideration, as they do not read on the elected species for component (b) or the elected invention.

3. Claims 1-2, 4-5, 8-22, 24, 26-31, and 34-35 were examined with regards to the elected compound of formula (V) of component (b) of the composition, (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea, and a compound of formula (I).

4. Claims 1-2, 4-5, 8-22, 24, 26-31, and 34-35 are rejected.

Claim Rejections-35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

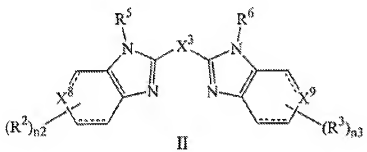
7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-2, 4-5, 8-22, 29-31, and 34-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Church et. al., WO 98/45275, in view of Carter et. al., WO 2004/026843 (international filing date 9/22/2003; publication date 4/1/2004; of previous record).

The claims are directed to a pharmaceutical composition comprised of the elected benzodiazepine compound of formula (V), (S)-1-(2-fluorophenyl)-3-(2-oxo-5-

phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea; and an inhibitor of the RSV fusion protein of formula (I).

Church et. al. teaches pharmaceutical compositions comprised of compounds which are useful for the treatment of mast-cell mediated inflammatory disorders and viral infections (Abstract). Treatment of syncytial viral infections, including respiratory syncytial virus, is taught (p. 6, lines 10-17; p. 12, lines 1-2; p. 22, lines 7-13; p. 22, line 28-p. 23, line 9; pp. 86-88, claim 1; p. 95, claim 24). The compounds taught by Church as effective for treating RSV that are also included within the group of compounds of formula (I) in the claimed composition are represented by the formula shown below (Abstract; p. 3, line 9-p. 5, line 28; p. 17, line 1-p. 18, line 31):



II

Where the dashed lines are independently bonds; R^2=C_{1-6} alkyl; R^3=C_{1-6} alkyl, halogen, or C_{1-6} alkyloxy; X^3=-CR^7R^8-; R^7=H or C_{1-6} alkyl; R^8=C_{1-6} alkyl; X^8=-$CH(R^1)_{n1}$, -$C(R^1)_{n1}$; R^1=-$C(NR^9)NR^9$ or -$(CR^{11}R^{11})_yNH_2$; R^9=H; R^{11}=H or C_{1-3} alkyl; y= 0 or 1; X^9=-$CH(R^4)$, -$C(R^4)$=, -N=, or –$N(R^4)$-; R^5=H, C_{1-4} alkyl; R^6=H, optionally substituted C_{1-6} alkyl; n1=0 or 1; n2=0 to 4; n3=0 to 4; R^3=C_{1-6} alkyl, C_{1-6} alkoxy, cyano, halo; R^4=-R^{12}; R^{12}=-R^{15} or –X^6-$(R^{15})_{n15}$; R^{15}=H; X^6=C_{1-6} alkylene; n15=1. Pharmaceutically acceptable salts are taught (p. 13, lines 6-24).

The compounds are effective in blocking cell fusion caused by a syncytial virus (p. 22, lines 24-26). The therapeutically effective amount of compound present per unit dosage form ranges from 0.01 to 1000 mg (p. 23, line 28-p. 24, line 2).

Church et. al. does not teach that the composition also comprises a benzodiazepine compound capable of inhibiting RSV replication, such as the elected compound of formula (V), (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea.

Carter et. al. teaches benzodiazepine compounds which have activity against RSV (Abstract; p. 1, lines 4-5, and line 19-p. 4, line 13). Pharmaceutically acceptable salts are taught (p. 18, line 27-p. 19, line 3), in addition to pharmaceutical compositions (p. 52, lines 19-27). Carter discloses the elected compound of formula (V), (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea, as a preferred RSV inhibitor (p. 19, line 4 and p. 23, lines 8-9; p. 89, Ex. 73b, lines 4-13). Pharmaceutical compositions are taught to comprise up to 85% by weight of the active compound (p. 37, lines 22-26).

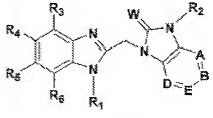
It would have been prima facie obvious to one of ordinary skill in the art, at the time of the invention, to have combined a compound of formula (I) as taught by Church et. al. with the elected benzodiazepine compound of formula (V), (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea, because both compounds are taught by the prior art to have efficacy for treating RSV. According to the MPEP 2144.05, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third

composition to be used for the very same purpose….[T]he idea of combining them flows logically from their having been individually taught in the prior art"; see *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). Church et. al. teaches that the compounds of formula (I), as discussed above, are useful for treating syncytial viruses, including respiratory syncytial virus; Carter et. al. teaches that the elected benzodiazepine compound of formula (V) is also effective against RSV. Therefore, one of ordinary skill in the art would have been motivated to have combined the compounds of formula (I) as taught by Church et. al. with the elected compound of formula (V), with the expectation that the combination would also have been effective against RSV. It would have been obvious that the composition comprised of a compound of formula (I) and the elected compound of formula (V), (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea , would have been suitable for simultaneous, sequential, or separate administration, depending upon the particular formulation, as both compounds of the composition are taught to be useful for treating RSV. While Church et. al. doesn't explicitly teach that the composition comprises between 0.025% to 10% by weight of a compound of formula (I), Church et. al. does teach therapeutically effective concentrations of the active drug in a pharmaceutical composition. It would thus have been obvious to have formulated the composition to have comprised between 0.025% to 10% by weight of a compound of formula (I), as this weight percent of the compound in a composition constitutes a therapeutically effective amount for treating RSV.

9. Claims 1-2, 4-5, 8-22, 24, 29-31, 34, and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et. al., WO 01/95910, in view of Carter et. al., WO 2004/026843 (international filing date 9/22/2003; publication date 4/1/2004; both references of previous record).

The claims are directed to a pharmaceutical composition comprised of a compound of formula (I) and the elected compound of formula (V) for component (b), (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea.

Yu et. al. teaches imidazopyridine and imidazopyrimidine compounds, and pharmaceutical compositions comprised of the compounds, for the treatment of respiratory syncytial virus infection (Abstract; p. 1, lines 8-11). Respiratory syncytial virus, or RSV, is a leading cause of serious lower respiratory infections in infants, children, elderly, and patients with compromised immune systems (p. 1, lines 15-26). The compounds taught by Yu et. al. as inhibitors of RSV that are structurally similar to the compounds of formula (I) of the claimed composition are represented by the formula shown below (p. 4, line 5-p. 9, line 3):



Formula I

Where W=O or S; R_1=-(CR'R")n-X; n=2 to 6; R', R"=independently H, C_{1-6} alkyl; X=H, C_{1-6} alkyl, NR'R", NR'COR", OR', COOR', CONR'R", aryl, heteroaryl, or heterocyclyl; A, B, D, E = independently C-H, C-Q-, or N, provided at least one of A, B, D, or E is not C-H or C-Q-; Q=halogen, C_{1-3} alkyl, or H; R_2=H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-6} cycloalkyl; R_3, R_4, R_5, R_6=independently H, C_{1-6} alkyl, or C_{1-6} alkyl substituted with halogen, OR', COOR', CONR'R". Pharmaceutically acceptable salts are also taught (p. 9, lines 10-23). Therapeutically effective dosages are taught to range from 0.1 to 100 mg/kg body weight, per dose (p. 186, line 25-p. 187, line 5). The compounds taught by Yu et. al. as presented above are very structurally similar to the compositions of formula (I) cited in the claimed composition. The compounds of formula (I) of the claimed composition include Z=CR_6R', where R_6=H, and R'=methyl; therefore, the cited compounds of formula (I) of the claimed composition include the linker Z=-$CH(CH_3)$-. The compounds taught by Yu et. al. have this equivalent position occupied by -(CH_2)-; the compounds of formula (I) cited in the claimed composition and the compounds taught by Yu et. al. as such only differ by the replacement of a hydrogen substituent for methyl. However, the replacement of hydrogen for methyl would have been expected by one of ordinary skill in the art, in the absence of unexpected results, to have resulted in a compound with similar properties and/or characteristics to the parent compound. According to the MPEP 2144.08, the substitution of hydrogen for methyl on otherwise structurally identical compounds would have been prima facie obvious to one of ordinary skill in the art; see *In re Druey*, 319 F.2d 237, 240, 138 USPQ 39, 41 (CCPA 1963). Yu et. al. teaches compounds which are nearly structurally identical to the compounds of formula

(I) as effective for treating RSV infection; therefore, it would have been prima facie obvious for one of ordinary skill in the art to have replaced the methylene linker of the compounds taught by Yu et. al. with -CH(CH_3)-, with the expectation that such an alteration would have resulted in compounds with similar properties and characteristics, as effective therapeutic agents for the treatment of RSV infection.

Yu et. al. does not teach that the composition also comprises the elected benzodiazepine compound of formula (V), (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea.

Carter et. al. teaches benzodiazepine compounds which have activity against RSV (Abstract; p. 1, lines 4-5, and line 19-p. 4, line 13). Pharmaceutically acceptable salts are taught (p. 18, line 27-p. 19, line 3), in addition to pharmaceutical compositions (p. 52, lines 19-27). Carter discloses the elected compound of formula (V), (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea, as a preferred RSV inhibitor (p. 19, line 4 and p. 23, lines 8-9; p. 89, Ex. 73b, lines 4-13). Pharmaceutical compositions are taught to comprise up to 85% by weight of the active compound (p. 37, lines 22-26).

It would have been prima facie obvious to one of ordinary skill in the art, at the time of the invention, to have combined a compound of formula (I) as prima facie obvious over Yu et. al. with the elected benzodiazepine compound of formula (V), (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea, because both compounds are taught by the prior art to have efficacy for treating RSV. According to the MPEP 2144.05, "It is prima facie obvious to combine two compositions

each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose....[T]he idea of combining them flows logically from their having been individually taught in the prior art"; see *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). Yu et. al. teaches that compounds structurally similar to those of formula (I), as discussed above, are useful for treating respiratory syncytial virus; Carter et. al. teaches that the elected benzodiazepine compound of formula (V) is also effective against RSV. Therefore, one of ordinary skill in the art would have been motivated to have combined the compounds of formula (I) as made obvious by Yu et. al. with the elected compound of formula (V), with the expectation that the combination would also have been effective against RSV. It would have been obvious that the composition comprised of a compound of formula (I) and the elected compound of formula (V), (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea , would have been suitable for simultaneous, sequential, or separate administration, depending upon the particular formulation, as both compounds of the composition are taught to be useful for treating RSV. While Yu et. al. doesn't explicitly teach that the composition comprises between 0.025% to 10% by weight of a compound of formula (I), Yu et. al. does teach therapeutically effective concentrations of the active RSV drug in a pharmaceutical composition. It would thus have been obvious to have formulated the composition to have comprised between 0.025% to 10% by weight of a compound of formula (I), as this weight percent of the compound in a composition constitutes a therapeutically effective amount for treating RSV.

Claim Rejections-35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

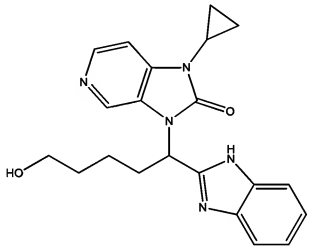
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 19, 24, and 26-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claim 19 recites the limitation of a composition according to claim 2 wherein the benzodiazepine of formula (V) is of formula (Va), wherein R^1=phenyl or methyl, and the phenyl moiety of R^1 being unsubstituted or substituted by a single fluorine, chlorine, C_{1-2} alkyl, C_{1-2} alkoxy, amino, etc. However, claim 2 does not cite that the phenyl of R^1 is optionally substituted; therefore, there is insufficient antecedent basis for this limitation in the claim. For purposes of providing compact prosecution and in searching for prior art, claim 19 was interpreted as R^1 including unsubstituted phenyl, which therefore includes the elected compound of formula (V), (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea.

13. Claim 24 recites the limitation of a composition according to claim 1, where Y includes CN, -NR'R", -COR', or $-SO_2R'$, in addition to other possible substituents; however, claim 1 does not cite that Y can be CN, -NR'R", -COR', or $-SO_2R'$. There is insufficient antecedent basis for this limitation in the claim.

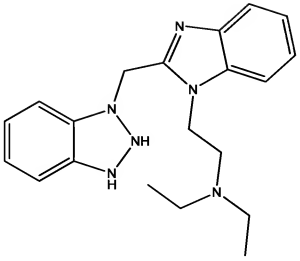
14. Claim 26 recites the composition according to claim 1, wherein component (a) is: 1-cyclopropyl-3-[1-(4-hydroxy-butyl)-1H-benzoimidazol-2-ylmethyl]-1,3-dihydro-imidazo[4,5-c]pyridine-2-one, shown below:



1-cyclopropyl-3-[1-(4-hydroxy-butyl)-1H-benzoimidazol-2-ylmethyl]-1,3-dihydro-imidazo[4,5-c]pyridin-2-one

For the above shown compound, Z is CR_6R', where R_6 is H, and R'=butyl substituted with hydroxyl. However, claim 1 does not cite that R' includes optionally substituted $C_{1\text{-}6}$ alkyl; therefore, therefore, there is insufficient antecedent basis for this limitation in the claim. Applicants are requested to amend independent claim 1 to include these particular limitations to overcome this rejection.

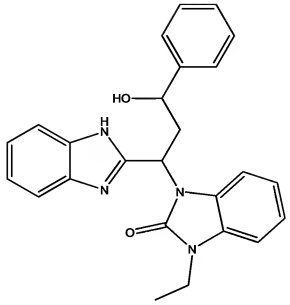
15. Claim 26 recites the composition according to claim 1, wherein component (a) is: {2-[2-(1,2-dihydro-benzotriazol-1-ylmethyl)-benzoimidazol-1-yl]-ethyl}-diethyl-amine, shown below:



{2-[2-(1,2-dihydro-benzotriazol-1-ylmethyl)-benzoimidazol-1-yl]ethyl}-diethyl-amine

However, claim 1 cites that for component (a) Z is CR_6R', where R_6 is H, or straight, branched or cyclic $C_{1\text{-}6}$ alkyl, and R' is straight, branched, or cyclic $C_{1\text{-}6}$ alkyl. For the compound shown above, both R_6 and R' are H; therefore, there is insufficient antecedent basis for this limitation in the claim.

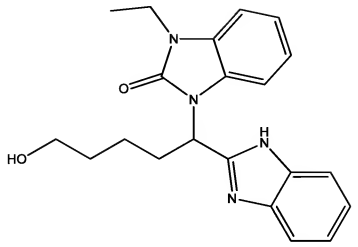
16. Claim 26 recites the composition according to claim 1, wherein component (a) is: 1-ethyl-3-[1-(2-hydroxy-2-phenyl-ethyl)-1H-benzoimidazol-2-ylmethyl]-1,3-dihydro-benzoimidazol-2-one, shown below:



1-ethyl-3-[1-(2-hydroxy-2-phenyl-ethyl)-1H-benzoimidazol-2-ylmethyl]-1,3-dihydro-benzoimidazol-2-one

For the compound shown above, Z is CR_6R', where R_6 is H, and R'=ethyl substituted with hydroxyl and phenyl. However, claim 1 does not cite that R' includes optionally substituted $C_{1\text{-}6}$ alkyl; therefore, therefore, there is insufficient antecedent basis for this limitation in the claim. Applicants are requested to amend independent claim 1 to include these particular limitations to overcome this rejection.

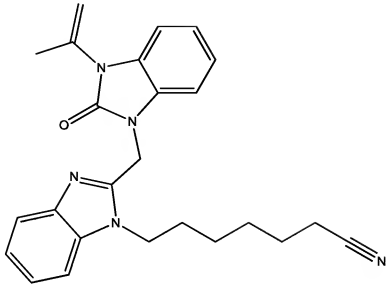
17. Claim 26 recites the composition according to claim 1, wherein component (a) is: 1-Ethyl-3-[1-(4-hydroxy-butyl)-1H-benzoimidazol-2-ylmethyl]-1,3-dihydro-benzoimidazol-2-one, shown below:



1-ethyl-3-[1-(4-hydroxy-butyl)-1H-benzoimidazol-2-ylmethyl]-1,3-dihydro-benzoimidazol-2-one

For the above shown compound, Z is CR_6R', where R_6 is H, and R'=butyl substituted with hydroxyl. However, claim 1 does not cite that R' includes optionally substituted C_{1-6} alkyl; therefore, therefore, there is insufficient antecedent basis for this limitation in the claim. Applicants are requested to amend independent claim 1 to include these particular limitations to overcome this rejection.

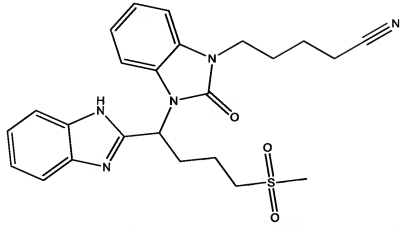
18. Claim 26 recites the composition according to claim 1, wherein component (a) is: 7-[2-(3-isopropenyl-2-oxo-2,3-dihydrobenzoimidazol-1-ylmethyl)-benzoimidazol-1-yl]-heptanenitrile, shown below:



7-[2-(3-isopropenyl-2-oxo-2,3-dihydrobenzoimidazol-1-ylmethyl)-benzoimidazol-1-yl]-heptanenitril

However, claim 1 cites that for component (a) Z is CR_6R', where R_6 is H, or straight, branched or cyclic C_{1-6} alkyl, and R' is straight, branched, or cyclic C_{1-6} alkyl. For the compound shown above, both R_6 and R' are H; therefore, there is insufficient antecedent basis for this limitation in the claim. Additionally, for the compound shown above, Y is R_4, where R_4 is heptyl substituted with nitrile; however, claim 1 does not cite that R_4 includes optionally substituted C_{1-6} alkyl.

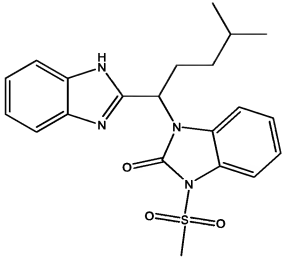
19. Claim 26 recites the composition according to claim 1, wherein component (a) is: 5-{3-[1-(3-methanesulfonyl-propyl)-1H-benzoimidazol-2-ylmethyl]-2-oxo-2,3-dihydro-benzoimidazol-1-yl}-pentanenitrile, shown below:



5-{3-[1-(3-methanesulfonyl-propyl)-1H-benzoimidazol-2-ylmethyl]-2-oxo-2,3-dihydro-benzoimidazol-1-yl}-pentanenitrile

For the above shown compound, Z is CR_6R', where R_6 is H, and R'=propyl substituted with methanesulfonyl. However, claim 1 does not cite that R' includes optionally substituted $C_{1\text{-}6}$ alkyl; therefore, there is insufficient antecedent basis for this limitation in the claim. Applicants are requested to amend independent claim 1 to include these particular limitations to overcome this rejection.

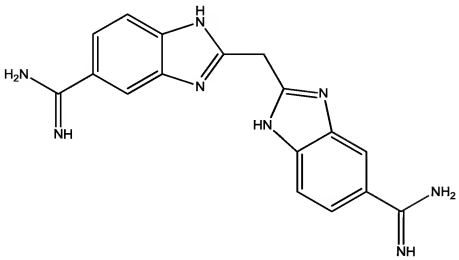
20. Claim 26 recites the composition according to claim 1, wherein component (a) is: 1-methanesulfonyl-3-[1-(3-methyl-butyl)-1H-benzoimidazol-2-ylmethyl]-1,3-dihydro-benzoimidazol-2-one, shown below:



1-methanesulfonyl-3-[1-(3-methyl-butyl)-1H-benzoimidazol-2-ylmethyl]-1,3-dihydro-benzoimidazol-2-one

For the above shown compound, A=N substituted with SO_2-CH_3; however, while claim 1 cites that A is optionally substituted with $SO_2NR_4R_5$, the substituent SO_2-CH_3 is not cited. There is insufficient antecedent basis for this limitation in the claim.

21. Claim 26 recites the composition according to claim 1, wherein component (a) is: Bis(5-amidino-2-benzimidazolyl)-methane, shown below:

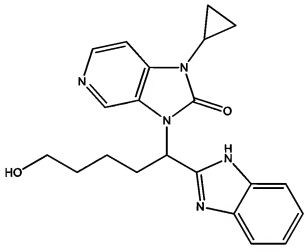


Bis(5-amidino-2-benzimidazolyl)-methane

For the above shown compound, both R_6 and R' are H; however, claim 1 does not cite that R' can be H. There is insufficient antecedent basis for this limitation in the claim.

22. Claim 26 recites the composition according to claim 1, wherein component (a) is: 2-{2-[1-[1-(2-amino-ethyl)-piperidin-4-ylamino]-4-methyl-benzoimidazol-1-ylmethyl}-6-methyl-pyridin-3-ol. However, this compound does not have the group Q present, where Q is the bicyclic heterocyclic ring structure specified in claim 1. Therefore, there is insufficient antecedent basis for this limitation in the claim.

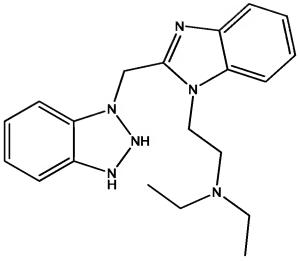
23. Claim 27 recites the composition according to claim 1, wherein component (a) is: 1-cyclopropyl-3-[1-(4-hydroxy-butyl)-1H-benzoimidazol-2-ylmethyl]-1,3-dihydro-imidazo[4,5-c]pyridine-2-one, shown below:



1-cyclopropyl-3-[1-(4-hydroxy-butyl)-1H-benzoimidazol-2-ylmethyl]-1,3-dihydro-imidazo[4,5-c]pyridin-2-one

For the above shown compound, Z is CR_6R', where R_6 is H, and R'=butyl substituted with hydroxyl. However, claim 1 does not cite that R' includes optionally substituted C_{1-6} alkyl; therefore, therefore, there is insufficient antecedent basis for this limitation in the claim. Applicants are requested to amend independent claim 1 to include these particular limitations to overcome this rejection.

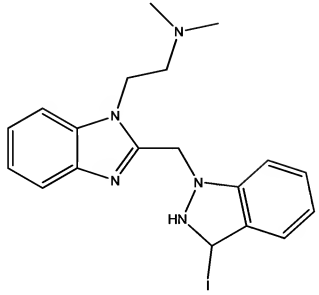
24. Claim 27 recites the composition according to claim 1, wherein component (a) is: {2-[2-(1,2-dihydro-benzotriazol-1-ylmethyl)-benzoimidazol-1-yl]ethyl}-diethyl-amine, shown below:



{2-[2-(1,2-dihydro-benzotriazol-1-ylmethyl)-benzoimidazol-1-yl]ethyl}-diethyl-amine

However, claim 1 cites that for component (a) Z is CR_6R', where R_6 is H, or straight, branched or cyclic $C_{1\text{-}6}$ alkyl, and R' is straight, branched, or cyclic $C_{1\text{-}6}$ alkyl. For the compound shown above, both R_6 and R' are H; therefore, there is insufficient antecedent basis for this limitation in the claim.

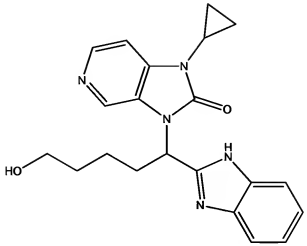
25. Claim 27 recites the composition according to claim 1, wherein component (a) is: {2-[2-(3-iodo-2,3-dihydro-indazol-1-ylmethyl)-benzimidazol-1-yl]-ethyl}-dimethyl-amine, shown below:



{2-[2-(3-iodo-2,3-dihydro-indazol-1-ylmethyl)-benzimidazol-1-yl]-ethyl}-dimethyl-amine

However, claim 1 cites that for component (a) Z is CR_6R', where R_6 is H, or straight, branched or cyclic C_{1-6} alkyl, and R' is straight, branched, or cyclic C_{1-6} alkyl. For the compound shown above, both R_6 and R' are H; therefore, there is insufficient antecedent basis for this limitation in the claim.

26. Claim 28 recites the composition according to claim 1, wherein component (a) is: 1-cyclopropyl-3-[1-(4-hydroxy-butyl)-1H-benzoimidazol-2-ylmethyl]-1,3-dihydro-imidazo[4,5-c]pyridine-2-one, shown below:



1-cyclopropyl-3-[1-(4-hydroxy-butyl)-1H-benzoimidazol-2-ylmethyl]-1,3-dihydro-imidazol[4,5-c]pyridin-2-one

For the above shown compound, Z is CR_6R', where R_6 is H, and R'=butyl substituted with hydroxyl. However, claim 1 does not cite that R' includes optionally substituted C_{1-6} alkyl; therefore, therefore, there is insufficient antecedent basis for this limitation in the claim. Applicants are requested to amend independent claim 1 to include these particular limitations to overcome this rejection.

Claim Rejections-Obviousness Type Double Patenting

27. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims

are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

28. Claims 1-2, 4-5, 8-22, 29-31, and 34-35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 7,582,624 in view of Church et. al., WO 98/45275. The claims of the US patent are directed to a compound of formula (Ic), which includes the compounds of formula (V) cited in the instantly claimed composition. While the claims of the US patent do not cite a pharmaceutical composition comprised of the compounds which also

includes compounds of formula (I) as instantly claimed, as the compounds cited in the claims of the US patent have medicinal utility, it would have been prima facie obvious to have formulated a pharmaceutical composition comprised of the compounds. Additionally, Church et. al. teaches a group of compounds of formula (I) as inhibitors of RSV (Abstract; p. 3, line 9-p. 5, line 28; p. 17, line 1-p. 18, line 31; p. 6, lines 10-17; p. 12, lines 1-2; p. 22, lines 7-13; p. 22, line 28-p. 23, line 9; pp. 86-88, claim 1; p. 95, claim 24). It would have therefore been prima facie obvious to have combined a compound of formula (I) with a benzodiazepine compound cited in the claims of the US patent, as both compounds have utility for treating RSV. According to the MPEP 2144.05, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose....[T]he idea of combining them flows logically from their having been individually taught in the prior art"; see *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). The claims of the US patent and the claims of the instant application are therefore not patentably distinct from each other.

29. **Claims 1-2, 4-5, 8-22, 24, 29-31, and 34-35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 7,582,624 in view of Yu et. al., WO 01/95910**. The claims of the US patent are directed to a compound of formula (Ic), which includes the compounds of formula (V) cited in the instantly claimed composition. While the claims of

the US patent do not cite a pharmaceutical composition comprised of the compounds which also includes compounds of formula (I) as instantly claimed, as the compounds cited in the claims of the US patent have medicinal utility, it would have been prima facie obvious to have formulated a pharmaceutical composition comprised of the compounds. Additionally, Yu et. al. teaches a group of compounds nearly identical to those of formula (I) as inhibitors of RSV (Abstract; p. 4, line 5-p. 9, line 3). The compounds of formula (I) of the claimed composition include $Z=CR_6R'$, where $R_6=H$, and R'=methyl; therefore, the cited compounds of formula (I) of the claimed composition include the linker $Z=-CH(CH_3)-$. The compounds taught by Yu et. al. have this equivalent position occupied by $-(CH_2)-$; the compounds of formula (I) cited in the claimed composition and the compounds taught by Yu et. al. as such only differ by the replacement of a hydrogen substituent for methyl. However, the replacement of hydrogen for methyl would have been expected by one of ordinary skill in the art, in the absence of unexpected results, to have resulted in a compound with similar properties and/or characteristics to the parent compound. According to the MPEP 2144.08, the substitution of hydrogen for methyl on otherwise structurally identical compounds would have been prima facie obvious to one of ordinary skill in the art; see *In re Druey*, 319 F.2d 237, 240, 138 USPQ 39, 41 (CCPA 1963). Yu et. al. teaches compounds which are nearly structurally identical to the compounds of formula (I) as effective for treating RSV infection; therefore, it would have been prima facie obvious for one of ordinary skill in the art to have replaced the methylene linker of the compounds taught by Yu et. al. with $-CH(CH_3)-$, with the expectation that such an alteration would have resulted in

compounds with similar properties and characteristics, as effective therapeutic agents for the treatment of RSV infection. It would have therefore been prima facie obvious to have combined a compound of formula (I) with a benzodiazepine compound cited in the claims of the US patent, as both compounds have utility for treating RSV. According to the MPEP 2144.05, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose....[T]he idea of combining them flows logically from their having been individually taught in the prior art"; see *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). The claims of the US patent and the claims of the instant application are therefore not patentably distinct from each other.

Conclusion

30. No claim is currently found allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARAH PIHONAK whose telephone number is (571)270-7710. The examiner can normally be reached on Monday-Thursday 7:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

S.P.

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627